

### **REMARKS**

Entry of this amendment is requested in order to place the application in condition for allowance. By way of this amendment, amendments are offered with respect to claims 1, 17, 19, 21 and 35. Claims 18, 30, 32-34 and 51 are canceled. Support for the amendments to claim 35 is found in the specification as filed at page 16, lines 2-6. Support for the other claim amendments is found within the claims as originally filed and as such, it is submitted that no new matter has been added by way of this amendment.

Claims 1-16, 19, 21-29, 31 and 35-50 stand rejected under 35 U.S.C. §102(e) as anticipated by Levinson (US 2002/0177167). Additionally, claims 35-50 stand rejected under 35 U.S.C. §102(b) as anticipated by Gester (WO 99/04361) using U.S. Patent No. 6,529,612 as an equivalent thereof. Lastly, claims 17, 20 and 30 stand rejected under 35 U.S.C. §103(a) over Levinson in view of admitted prior art found on page 15 of the specification and page 24 of the specification, specifically including Moloshok et al. and Carter Jr. et al.

#### **Remarks Directed to Rejection of Pending Claims 1-16, 18, 19, 21-29, 31 and 33-50 under 35 U.S.C. §102(e) as Anticipated by Levinson (US 2002/0177167)**

It is stated in Paper No. 09202006, page 9, section 6, that "Applicant's amended changes to differentiate currently what was claimed in claims 1 and 35 do not overcome the prior art since Levinson 167 teaches said limitation which can be understood from the abstract and Sections 0023-0024 of the specification".

In contrast to the invention of independent claims 1, 21 and 35, the abstract of Levinson et al. discloses a method for determining *chemical compositions* and systems which include databases of molecular descriptors and related compounds and their properties as determined

empirically and through simulation, along with multidimensional visualization tools. Thus, the abstract does not disclose a process or system related to *crystallization parameter optimization*.

Paragraph [0023] of Levinson et al. reads in part:

In another aspect, the invention comprises a system for determining a solid form of a compound comprising: (1) a database comprising at least one table, the at least one table further comprising: (a) a plurality of molecular descriptors, (b) a plurality of compound identifiers, . . . (2) a query system for selecting subsets of related information from the at least one table; (3) a multidimensional representation generation module capable of generating visual representations of data sets having at least four dimensions; (4) a plurality of modeling modules, each module capable of receiving information selected by the query system and estimating at least one *property* of a formulation. (emphasis added)

Applicant submits that one skilled in the art would appreciate that a property is not a parameter. A property of an object is some intrinsic or extrinsic quality of that object. For example, a physical property of an object is any aspect of the object that can be measured or perceived without changing its identity -- a physical quantity that directly describes a physical attribute of the object. A parameter is a combination of the properties of an object which suffice to determine the response of the object. Properties have units of dimension whereas parameters are dimensionless. Applicant further submits that a property of a formulation is not equivalent to an optimal physical crystallization parameter. Therefore, the system of Levinson used to estimate at least one *property* of a formulation does not anticipate the method or system of the present invention used to determine optimal crystallization *parameters* of an unknown crystallization sample.

Paragraph [0024] of Levinson et al. reads:

In another aspect, the invention comprises a method for producing crystals comprising electronically calculating a set of predicted crystal polymorphs of a target compound; electronically calculating expected experimental results for the predicted crystal polymorphs; conducting a first plurality of crystallization

experiments using a high-throughput automated experimentation apparatus; *electronically comparing the expected experimental results with the actual experimental results to determine which predicted crystal polymorphs were produced.* (emphasis added)

Applicant submits that Levinson teaches one skilled in the art to compare which crystal structures actually formed after a series of experiments to which crystal structures were predicted. The present invention does not compare which crystal structures actually formed to which crystal structures were predicted. Rather, the independent claims 1, 21 and 35 pending recite a crystallization parameter optimization process wherein a predictive crystallization function is trained through analysis of a plurality of crystallization experimental samples and a plurality of physical characterization input variables. Furthermore, Levinson et al. does not disclose an incomplete factorial screen program having said predictive crystallization function.

In response to the rejection of claims 1-16, 19, 21-29, 31 and 35-50 as being anticipated by Levinson (US 2002/0177167), Applicant incorporates by reference the remarks stated in the Amendment in Response to Non-final Office Action mailed September 5, 2006. In summary, Applicant respectfully submits that Levinson et al. while teaching an extrapolative process fails to provide a teaching commensurate with the claim recitation of “training a predictive crystallization function ...” The extrapolative models of Levinson et al. are detailed in paragraphs [0150]-[0154]. Applicant submits that the regression methods detailed in the aforementioned paragraphs of Levinson et al. are able to fill in a missing result or extrapolate a trend from a string of results. This is in stark contrast to the inventive training exemplified in Examples 1 and 2 of the pending application (pages 24-35). Support for Applicant’s position is found in the fact that per Example 1 (page 24, line 13) a multi-step regression analysis comparable to that of Levinson et al. (see [0151] for “stepwise linear regression”) and one

performed yielded an R superscript value of only 0.54 indicative of nonconvergence (see instant specification, page 26, lines 6-10) whereas the neural network converged to a R superscript value of 0.754 (page 29, line 3) and a Chernov analysis converged to a R superscript value of 0.93 (page 30, lines 1-2). As such, Applicant submits that the predictive crystallization function is trained according to independent claims 1, 21 and 35 is not equivalent to the regression methodologies of Levinson et al. and as such these independent claims and those that depend therefrom are not anticipated by Levinson et al.

To further emphasize distinctions of the claimed invention relative to Levinson et al., claim 1 has been amended to incorporate the subject matter of original claim 18. As Levinson et al. nowhere contemplates "converting to vectors said plurality of crystallographic experimental samples," and thereafter training the predictive crystallization function, Applicant submits that claim 1 and those claims that depend therefrom this recitation provides an additional basis for novelty over Levinson et al. In the event that the rejection of independent claim 1 is maintained over Levinson et al., it is respectfully requested that the passages of Levinson et al. that recite converting the crystallization experimental samples to vectors prior to training be stated with specificity. In light of these remarks, reconsideration and withdrawal of the rejection as to claims 1-16, 19, 21-29, 31 and 35-50 under 35 U.S.C. §102(e) as anticipated by Levinson is requested.

**Remarks Directed to Rejection of Claims 35-50  
under 35 U.S.C. §102(b) as Anticipated by Gester (WO 99/04361)**

In response to the rejection of claims 35-50 as being anticipated by Gester (WO 99/04361) Applicant incorporates by reference the remarks stated in the Amendment in Response to Non-final Office Action mailed September 5, 2006.

In order to emphasize the computational attributes of the system embodied in claim 35, claim 35 has been amended to recite that the program performs “an operative algorithm selected from the group consisting of: a Chernov algorithm, a Mahalanobis distance and a Gram-Schmidt algorithm” as part of the parameter optimization routine. As the operation of the program modifies experiments performed by the manufacturing execution system and draws from a database to perform program operation on the computer, Applicant submits that the invention of claim 35 satisfies the requirements of an operational system as is supported in the instant specification at page 14, lines 1-12 that detail the interaction between computational software and hardware as embodied in pending claim 35. As Gester et al. is wholly silent as to Chernov algorithms, a Mahalanobis distance or a Gram-Schmidt algorithm as a basis for crystallization parameter analysis, Applicant submits that pending claim 35 and those claims that depend therefrom are not anticipated by Gester et al. In light of these remarks, reconsideration and withdrawal of the rejection as to claims 35-50 under 35 U.S.C. §102(b) as anticipated by Gester is requested.

**Remarks Directed to Rejection of Claims 17 and 20 under 35 U.S.C. §103(a)**

In response to the rejection of claims 17 and 20 as being obvious over Levinson in view of admitted prior art found on page 15 of the specification and page 24 of the specification, specifically including Moloshok et al. and Carter Jr. et al., Applicant incorporates by reference the remarks stated in the Amendment in Response to Non-final Office Action mailed September 5, 2006.

By way of this amendment, claim 17 has been rendered in independent form while independent claim 21 incorporates the subject matter of now canceled claim 30. In addition to the remarks made of record in the previous amendment, Applicant submits that Levinson et al. is

silent as to performing the Chernov analyses of pending claim 17 and 21, as well as the Markush group of analyses provided in pending claim 20. Applicant submits that reliance on secondary references found in the pending specification at pages 15 and 24 are misplaced. With respect to the teaching of Moloshok et al. (a copy of which is enclosed herewith), Applicant submits that Levinson et al. teaches away from application of Bayesian decomposition based on the teachings found in paragraph [0151]. Additionally, as Moloshok et al. only contemplates the use of Bayesian decomposition for the analysis of microarray data, one of ordinary skill in the art upon viewing Levinson et al. and Moloshok et al. is respectfully submitted to lack a motivation to apply Bayesian decomposition to the process of crystallization parameter optimization. In other words, a fair reading of Levinson et al. would not lead one to consider Bayesian decomposition as the results generated therein are inextricably linked with the microarray experiments performed. Additionally, the statement found in the last paragraph of page 573 of Moloshok et al. states "The ability to add additional prior knowledge through a convolution function ... in BD is a powerful tool which has not yet been exploited in expression analysis." Applicant respectfully submits that this statement at best represents a motivation to try the analysis performed by the claimed invention found in claim 20. It is well-established law that "obvious to try" is an improper basis for an obviousness-type rejection.

As Levinson et al. is silent as to a Chernov analysis per pending claims 17 and 21, a teaching sufficient to support a *prima facie* case of obviousness therefore must be found in one of the secondary references of Moloshok et al. or one of the Carter et al. references referenced in the specification at page 24. It is respectfully submitted that Moloshok et al. is wholly silent as to the performing of a Chernov analysis, as are the Carter references. Rather, the Carter references provided on page 24 of the instant specification relate to the conventional multi-step

regression analysis that is readily conceded to be prior art and indeed shown to be nonfunctional (see page 26, line 6 of the specification). Indeed, the teachings of the Carter references are commensurate in scope with the regression methods detailed in Levinson et al. at paragraph [0151]. As such, it is respectfully submitted that a *prima facie* case of obviousness as to pending claims 17, 20 and 21 cannot be sustained.

In light of the above amendments, reconsideration and withdrawal of the rejection as to claims 17, 20 and 30 under 35 U.S.C. §103(a) over Levinson in view of admitted prior art is requested.

Summary

With this entry of this amendment, claims 1-17, 19-29, 31 and 35-50 remain pending for consideration. The outstanding rejections are believed to have been overcome. Should the Examiner have any suggestions as to how to improve the form of any of the pending claims, it is respectfully requested that the undersigned attorney in charge of this application be contacted to resolve any outstanding issues.

Dated:

Respectfully submitted,

By /Avery N. Goldstein, Ph.D./

Avery N. Goldstein, Ph.D.

Registration No.: 39,204

GIFFORD, KRASS, GROH, SPRINKLE,

ANDERSON & CITKOWSKI, P.C.

2701 Troy Center Drive, Suite 330

Post Office Box 7021

Troy, Michigan 48007-7021

(248) 647-6000

(248) 647-5210 (Fax)

Attorney for Applicant

Enclosure